

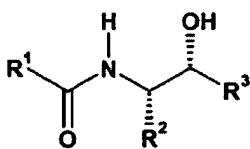
Remarks

Claims 1 and 6 - 9 remain pending in this application. The Examiner has required restriction of the pending claims under 35 U.S.C. 121 and 372. Claims 7 and 8 have been cancelled. Claim 1 has been amended to comply with the restriction requirement.

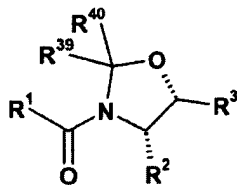
Restrictions/Election of Species

The Examiner has required restriction of the invention as originally claimed. The Examiner has asserted that the present application contains multiple inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. The Examiner has further asserted that there is no technical feature common to all the claims because the claims embrace structurally different heterocyclic cores (e.g., formula I - drawn to acyclic nitrogen- and oxygen-containing compounds and formula IV - drawn to cyclic nitrogen and oxygen containing compounds).

Claims 7 and 8 have been canceled. The cancellation of Claim 8 in the Amendments to the Claims has specifically addressed the Examiner's concerns of why the groups lack unity with each other: formula I - drawn to acyclic nitrogen- and oxygen-containing compounds and formula IV - drawn to cyclic nitrogen and oxygen-containing compounds. See below.



formula I



formula IV

As such, by cancelling Claim 8, the invention is drawn only around formula I and acyclic nitrogen- and oxygen-containing compounds. Further, Applicants have amended Claim 1 to substantially comply with the restriction requirement. However, Applicants wish to point out that R³ has been expanded to include the piperidin-2-yl moiety of formula a and b or a tetrahydropyridin-2-yl moiety of formula c and d of Group I and the piperazin-2-yl of Group II. The Examiner required restriction of Groups I and II. Applicants assert that the combination of Group I and Group II represents a single inventive concept for which a special technical feature exists and places no undue burden on the Examiner for searching or examination. Therefore, Applicants respectfully traverse this restriction.

The present application is an international application which has entered the U.S. national stage under 35 U.S.C. § 351. Restriction is therefore governed by unity of invention. MPEP

1893.03(d). Applicants assert that there is a technical relationship among the claimed inventions involving a special technical feature, especially between Groups I and II, and therefore unity of invention does exist. Furthermore, in the Written Opinion of the International Searching Authority, there was no issue of lack of unity of invention as presented here.

According to PCT Rule 13.2, unity of invention is "fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features." PCT Rule 13.2. The expression "special technical features" is defined as those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. *Id.*

Additional guidance relating to unity of invention is provided for Markush practice in section (f) of Annex B of the Administrative Instructions Under the Patent Cooperation Treaty. A copy is attached to this response for the Examiner's convenience. Section (f) states that the requirement of a technical interrelationship and the same or corresponding special technical features as defined in Rule 13.2, shall be met when the alternatives are of a similar nature:

(i) When the Markush grouping is for alternatives of chemical compounds, they shall be regarded as being of a similar nature where the following criteria are fulfilled:

(A) all alternatives have a common property or activity, *and*

(B)(1) a common structure is present, i.e., a significant structural element is shared by all of the alternatives, *or*

(B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains. (emphasis added)

(ii) In paragraph (f)(i)(B)(1), above, the words "significant structural element is shared by all of the alternatives" refer to cases where the compounds share a common chemical structure which occupies a large portion of their structures, or in case the compounds have in common only a small portion of their structures, the commonly shared structure constitutes a structurally distinctive portion in view of existing prior art, and the common structure is essential to the common property or activity. The structural element may be a single component or a combination of individual components linked together.

(iii) In paragraph (f)(i)(B)(2), above, the words "recognized class of chemical compounds" mean that there is an expectation from the knowledge in the art that members of the class will behave in the same way in the context of the claimed invention. In other words, each member could be substituted one for the other, with the expectation that the same intended result would be achieved.

(iv) The fact that the alternatives of a Markush grouping can be differently classified shall not, taken alone, be considered to be justification for a finding of a lack of unity of invention.

Administrative Instructions Under the Patent Cooperation Treaty, Annex B, pages 65-66.

Applicants assert that a special technical feature exists for Groups I and II. Pursuant to section (f)(i)(A) of Annex B, the Markush grouping is of a similar nature because the compounds of the formula provided all have a common property of activity of being useful as BACE inhibitors. Further, pursuant to section (f)(i)(B)(1), Applicants assert that all of the alternatives of chemical compounds possess a significant structural element, as shown by Figures (1) – (3) below.

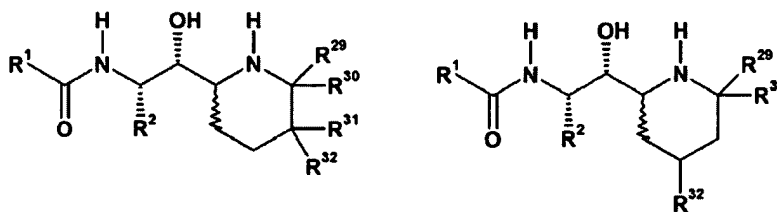


Figure (1)

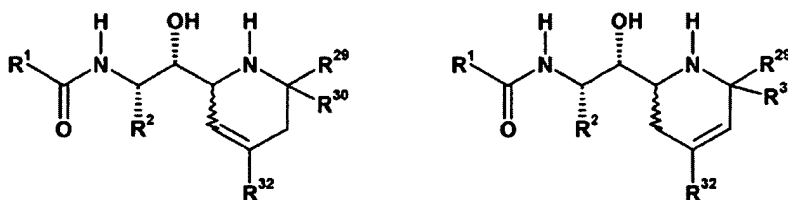


Figure (2)

Figures (1) and (2) represent Group I wherein R³ is a piperidin-2-yl moiety of formula a and b or a tetrahydropyridin-2-yl moiety of formula c and d.

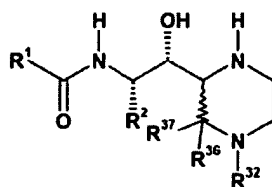


Figure (3)

Figure (3) represents Group II wherein R³ is piperazin-2-yl.

Applicants direct Examiner to section (f)(ii) wherein "significant structural element is shared by all of the alternatives" is defined as "where the compounds share a common chemical structure which occupies a large portion of their structures." *Id.* Groups I and II share a common core, as shown below in Figure (4), consisting of a 6 atom nitrogen-containing ring (E), wherein Z is CH₂ or CHR³² or NR³⁵, and a 4-component linker of -C(O)-, -N(H)-, -C(H)(R²)-, and -C(H)(OH)-, represented by A, B, C, and D, respectively.

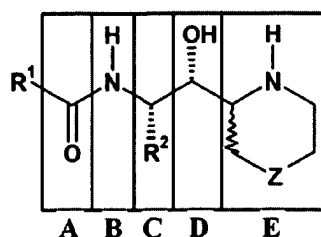


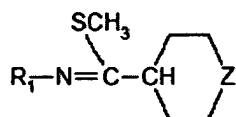
Figure (4)

Examiner has specifically restricted the invention drawn around the R^3 substituent, represented by E in Figure (4) above. Although Group I is directed to the piperidin-2-yl and tetrahydropyridin-2-yl moieties and Group II is directed to the piperazin-2-yl moiety, applicants direct Examiner to section (f)(iv) which states “the fact that the alternatives of a Markush grouping can be differently classified shall not, taken alone, be considered to be justification for a finding of a lack of unity of invention.” *Id.*

Applicants further direct Examiner to the PCT International Search and Preliminary Examination Guidelines, Part III, Chapter 10 Unity of Invention, Example 19, page 85, Figure (5) below (emphasis added). A copy is attached to this response for Examiner’s convenience. Example 19 illustrates an example of common structure in Markush practice directly on-point with the current invention. In Example 19, there is a significant structural element shared by all the alternatives – the iminothioether group linked to a six atom ring *which allows different heteroatom substitution*. Further, all claimed compounds are alleged to possess the same use. Therefore, unity of invention is present.

10.39 Example 19: common structure:

Claim 1: A compound of the formula:



wherein R_1 is selected from the group consisting of phenyl, pyridyl, thiazolyl, triazinyl, alkylthio, alkoxy, and methyl; Z is selected from the group consisting of oxygen (O), sulfur (S), imino (NH), and methylene ($-CH_2-$).

The compounds are alleged to be useful as pharmaceuticals for relieving lower back pain.

In this particular case the iminothioether group $-N=C-SCH_3$ linked to a six atom ring is the significant structural element which is shared by all the alternatives. Thus, since all the claimed compounds are alleged to possess the same use, unity would be present.

Figure (5)

Upon a comparison of the present invention as represented by Groups I and II, Figure (6) below, and Example 19 from the PCT International Search and Preliminary Examination Guidelines, Figure (7) below, an analogous situation arises. As in Example 19, all alternatives of Groups I and II share a significant structural element – the 4-component linker [as defined above in Figure (4)] connected to a six atom ring. Further, as in Example 19, the alternatives of Groups I and II possess the same use – BACE activity. Accordingly, Applicants assert that the same conclusion must be reached – unity of invention is present.

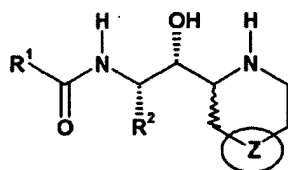


Figure (6)

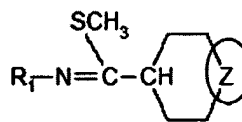


Figure (7)

Therefore, because the alternatives of the present Markush grouping, as represented by Groups I and II by the Examiner, have a common property of activity as BACE inhibitors and because they share a common chemical structure which occupies a large portion of their structures, Applicants assert that Groups I and II form a single general inventive concept under PCT Rule 13.1 and contain the same or corresponding technical features under PCT Rule 13.2, thereby meeting the criteria of unity of invention. As such, Applicants respectfully request that the restriction requirement be removed from Groups I and II.

In order for the response to be complete, applicants elect the species of Example 16, N-((1S,2R)-1-Benzyl-2-hydroxy-2-(R)-piperidin-2-ylethyl)-acetamide hydrochloride, Figure (8), below, to be examined. The elected species is encompassed by pending claims 1, 6, and 9.

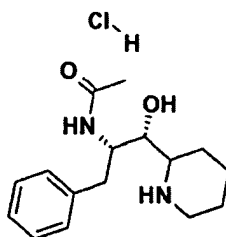


Figure (8)

In the event that Examiner does not withdraw the restriction requirement in view of the amendment and discussion, supra, and in order to be responsive, Applicants elect Group I with traverse. The same species as illustrated in Figure (8) above is selected to be examined. The elected species is encompassed by pending claims 1, 6, and 9.

Applicants will amend inventorship, if necessary, once claims are allowed.

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In summary, Applicants have canceled Claims 7 and 8 and amended Claim 1 to comply with the restriction requirement. Traversing the restriction requirement, Applicants assert that Groups I and II meet the unity of invention requirements and respectfully request that the restriction be removed.

Respectfully submitted,

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Attachments:

Administrative Instructions Under the Patent Cooperation Treaty, Annex B, November 26, 2008
PCT International Search and Preliminary Examination Guidelines, Part III, Chapter 10, March 11, 2004